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SHERIDAN ROSS PC
1560 BROADWAY
SUITE 1200
DENVER, CO 80202

EXAMINER	
LIU, SAMUEL W	
ART UNIT	**PAPER NUMBER**
1653	

DATE MAILED: 05/15/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/723,247	BAR-OR, DAVID	
	Examiner	Art Unit	
	Samuel W. Liu	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *6/27/06*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-185* is/are pending in the application.

4a) Of the above claim(s) *1-45,54-61,63-66,73,75-78 and 82-184* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *46-53,67-72,74,79-81 and 185* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *6/28/04 & 5/31/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of the claims

Claims 1-185 are pending.

The preliminary amendment filed 6/28/04, which adds claims 183-185, amends claims 22-23, 32-35, 68, 78, 97, 101, 103, 111, 113, 122, 124, 135, 137, 147, 149, 160, 162, 178, 180, and cancels claims 75-77 (the 2nd occurrence of claims 75-77 is canceled but the 1st occurrence of claims 75-77 remains, see below), has been entered.

IDS

The references cited in the IDS filed 6/28/04 and the IDS filed 5/31/05 have been considered by Examiner.

Election/Restrictions

Applicants' election (filed 4/27/06) of Group 3, claims 46-75 and 79-81 and election of phosvitin with traverse is acknowledged. The traversal is on the ground(s) that the Examiner's "additional elections" are inappropriate as the phosphate acceptor compounds (PACs), extracellular PACs (EPACs) and intracellular PACs (IPACs), which fall within Markush group, share common functional feature –they act as phosphate accepting molecules although they are structurally distinct (see page 3 of the response). The response also argue that the additional election requirement is inappropriate as they do not provide any indication as to how the claims are to be treated will be reviewed, withdrawn or cancelled based on any response by applicants (see page 2, the 3rd paragraph of the response).

The applicants' arguments are found to be unpersuasive because of the reasons set forth in the Office action mailed 3/27/06 and as follows.

Acceding to the definition of "*phosphate acceptor compound*" (page 4, lines 12-15 of the specification), the phosphate acceptor compound (PAC) is a compound that is capable of being phosphorylated", chemical structures and/or biological functions of PAC molecules, e.g., extracellular PAC (EPAC) and intracellular PAC (IPAC) as recited in the claims are widely diverse. Any nucleoside which is structurally distinct from polypeptide play essential role in biosynthesis of the corresponding nucleotide for nucleic acid synthesis besides that nucleoside can act as a phosphate acceptor; e.g., a nucleoside compound, uridylyl-(3'-5')-3-ribosyl-6-methyluracil (UprmU) can act as a PAC (see Kavunenko et al. (1976) *Nucleic Acids Res.* 3, 1073-101079).

As polypeptide PAC concerned, PAC molecule, e.g., Casein and albumin, in this application, are structurally and functional distinct proteins. Thus, the PAC, EPAC and IPAC molecules do not fall within the Markush group because said molecules are not related as species in view of structure and function. As discussed in the Office action mailed 3/27/06, the "additional election" under 35 USC 121 (1) is not a species election, and the election requirement is proper. The claims drawn to non-elected subject matter, e.g., protein/polypeptide which is not phosvitin, are withdrawn from further consideration. The requirement is therefore still deemed proper and is therefore made FINAL.

It is of note that there appears a "contradictory statement" in pages 8-9 of the "Amendment to the claims" filed 6/28/04, i.e., pages 8-9 set forth that claims 75-77 are pending while the same pages also states that claims 75-77 are canceled. However, in view of the applicant's "*Remarks*" filed 6/28/04 where applicant explicitly states that "there are *two incidences* (the **1st** occurrence and the **2nd** occurrence) of claims numbered as 75, 76 and 77 in the

original application" and that new claims 183, 184 and 185 are substituted for the canceled the 2nd occurrence of claims 75, 76 and 77, it is clear that claims 1-185 are pending.

Claims 1-45, 78 and 82-185 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

In addition, claims 54-56 which are drawn into non-elected casein, claim 57-58 which are drawn into non-elected albumin, and claim 63 which is drawn into the casein kinase substrate having amino acid sequence of SEQ ID NO:3 or 4 which both do NOT read on the elected phosvitin amino acid sequence (see Byrne et al. (1984) *Biochemistry*, 23, 4275-4279) are withdrawn from further consideration. Claim 61 is directed to "a mixture of plasma protein" which is drawn to non-elected invention because applicant has elected phosvitin, which is not the mixture of plasma protein, for examination. Claims 64-66 are directed to a synthetic peptide; since the elected phosvitin is not the chemically synthesized but rather is a naturally occurring chicken egg yolk protein, claims 64-66 are drawn to non-elected invention. For the same reason, claims 75-77 are withdrawn from further consideration as being directed to the non-elected invention.

The peptide having the structure set forth in claims 59 and 73 does not read on the phosvitin amino acid sequence (see Figure 4, Byrne et al.); and thus claims 59 and 73 and claim 60 (depending from claim 59) are withdrawn from further consideration.

Further, new claims 183-184, the process claims, are drawn to the nonelected invention.

Therefore, the pending claims 46-53, 67-72, 74, 79-81 and 185 together with the elected phosvitin are under examination to the extent that they are drawn to the elected invention.

Specification/claim Objection

The disclosure is objected to because of the following informalities:

(1) On page 64, line11,"BSA" and "ELIS" and line 19, "ELISA" should be spelled out in full for the first instance of use.

(2) On page 6, line 2, page 9, line 6, page 12, line 12, and page 14, line 28, the specification sets forth http://www.cbs.dut.dk/databases/PhosphoBase/", http://www.worthington-biochem.com/CASA, http://www.cbs.dtu.dk/databases/Phospho Base/, and http://www.cbs.dtu.dk/databases/Phospho Base/, respectively. The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP §608.01. Note that the embedded hyperlinks and/or other forms of browser-executable code are impermissible and require deletion. The attempt to incorporate subject matter into the patent application by reference to a hyperlink and/or other forms of browser-executable code is considered to be an improper incorporation by reference. See MPEP § 608.01(p), paragraph I regarding incorporation by reference. If the application attempts to incorporate essential or nonessential subject matter into the patent application by reference to the contents of the site to which a hyperlink and/or other form of browser-executable code is directed, use form paragraph 6.19 or 6.19.01 instead. See also MPEP § 608.01(p). for example, applicants may want to have the "http://" removed because it is this element that makes the link active. The remainder of the hyperlink can be and should be left behind.

(3) In claim 80, "EPACs" should be spelled out for the first time recitation in the claims.

Claim Rejections - 35 USC § 112, the second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter that the applicant regards as his invention.

Claims 67, 76, 81 and 185 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 67 and 185 recite "*attached to*"; the recitation is unclear whether or not it refers to "covalently linked to" or "non-covalently associated with". The specification does not define this recitation. It is of note that, on page 48, lines 9-13, the specification sets forth "...bound to, attached to, entrapped in..." but the specification does not clearly indicate whether or not "attached to" refers to covalently or non-covalently attached to.

Claim 76 is indefinite in "*a random sequence*" because it is unclear whether or not the "random sequence" refers to any combination of amino acids derived from the PAC polypeptide/peptide or any fragments or subsequences thereof. The specification does not define what the *random sequence* is.

Claim 81 recites the non-elected subject matter ""a combination of EPACs" and "other EPAC(s)" which are drawn to non-elected invention because the "EPACs" and "EPAC(s)" are not directed to the elected phosvitin polypeptide; said recitation thus render the claim indefinite.

Claim Rejections - 35 USC §102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 46-49, 62, 67-70, 72, 74, 79 and 185 are rejected under 35 U.S.C. 102(b) as being anticipated by Istituto Farmacologico Serono [**IFS**](GB1350197) as is evidenced by Fujino et al. (*Gamete Res.* (1983) 7, 429-257) who teach that the naturally occurring phosvitin is not fully phosphorylated.

In the patent claim 1, IFS discloses a pharmaceutical composition comprising phosvitin, which anticipates instant claims 46-47.

In Example 3, IFS teaches that the phosvitin is prepared from hen's egg yolk (see page 3, the left column, line 3), which anticipates instant claim 49.

Since naturally-occurring phosvitin has inherent property, i.e., the phosvitin is a substrate of a phosvitin-specific kinase (see page 255 and Table 3 of Fujino et al.), indicating that the phosvitin is not fully phosphorylated polypeptide (i.e., partially phosphorylated), and thus is a phosphate acceptor, the above teaching anticipates instant claims 48, 62 and 74.

Since naturally occurring phosvitin is a substrate of a phosvitin specific kinase indicating that the phosvitin is not fully phosphorylated polypeptide (i.e., partially phosphorylated), and thus is a phosphate acceptor, the above teaching anticipates instant claims 48, 62 and 74.

On page 1, the left column, line 29, IFS Caprino teaches iron-phosvitin complex, i.e., the phosvitin protein has inherent property of binding with iron molecule (target molecules) through its negatively-charged phosphate groups; and thus, the above IFS's teachings anticipate instant claims 67 and 185.

On page 3, the right column, lines 70-75, IFS teaches intramuscular administration of the pharmaceutical composition to a subject, which anticipates instant claim 68.

Claim 69 recitation "*is suitable for topical administration of the EPAC to the skin*" is considered to an intended use which has little patent weight, and thus, the above IFS ' teachings anticipate instant claim 69.

In Example 4, IFS teaches that the pharmaceutical composition is prepared in solution, which anticipates instant claim 70.

Since the claim 79 recitation "for contacting ..." is an intended use which has no patent weight for the claimed composition; and thus, the above IFS' teachings anticipate instant claim 79.

Since both "extracellular" and "intracellular" (for PAC) are considered to be an intended use which has no patentable weight for the claimed composition, the above IFS' teachings anticipate instant claim 72.

Claims 46-49, 62, 67-70, 72, 74, 79 and 185 are rejected under 35 U.S.C. 102(b) as being anticipated by Caprino L. (US Pat. No. 3966915) as is evidenced by Fujino et al. teaching that the naturally occurring phosvitin is not fully phosphorylated (*Gamete Res.* (1983) 7, 429-257).

In Example 3, Caprino discloses a pharmaceutical composition comprising phosvitin, which anticipates instant claims 46-47.

In Example 3 (column 3, line 32), Caprino teaches that the phosvitin is prepared from hen's egg yolk (see page 3, the left column, line 3), which anticipates instant claim 49.

Since naturally-occurring phosvitin has inherent property, i.e., the phosvitin is a substrate of a phosvitin-specific kinase (see page 255 and Table 3 of Fujino et al.), indicating that the phosvitin is not fully phosphorylated polypeptide (i.e., partially phosphorylated), and thus is a phosphate acceptor, the above teaching anticipates instant claims 48, 62 and 74.

In Example 3, Caprino teaches intramuscular administration of the pharmaceutical composition to a subject, which anticipates instant claim 68.

Since claim 69 recitation "*is suitable for topical administration of the EPAC to the skin*" is considered to an intended use which has little patent weight, and thus, the Caprino' teachings anticipate instant claim 69.

In Example 3, Caprino teaches that the pharmaceutical composition is prepared in a solution, which anticipates instant claim 70.

Since the recitation of claims 67 and 185 "wherein the EPAC is attached to a targeting molecule " is an intended use which has no patent weight for the claimed composition; and thus, the Caprino's teachings anticipate instant claims 67 and 185.

Since the claim 79 recitation "*for contacting* ..." is an intended use which has no patent weight for the claimed composition; and thus, the above Caprino's teachings anticipate instant claim 79.

Since both "extracellular" and "intracellular" (for PAC) are considered to be an intended use which has no patentable weight for the claimed composition, the Caprino's teachings anticipate instant claim 72.

On column 1, line 22, Caprino teaches ion-phosvitin complex, i.e., the phosvitin protein has inherent property of binding with iron molecule (target molecules) through its negatively

charged phosphate groups; and thus, the above Caprino's teachings anticipate instant claims 67 and 185.

Claims 46-53, 62, 72, 74 and 79-80 are rejected under 35 U.S.C. 102(b) as being anticipated by Jiang et al. (*J. Agric. Food Chem.* (2000) 48, 990-994).

On "Materials and Methods" section, Jiang teach a preparation comprising alkaline-dephosphorylated phosvitin wherein the dephosphorylated phosvitin is dissolved in Milli-Q pure water (see page 991, the left column, the last paragraph, the 1st sentence) of pH adjusted to 8.0. Such the phosvitin-dissolved solution is considered to be a pharmaceutical composition which anticipates instant claims 46-48.

The phosvitin is obtained from hen (see page 991, the left column, line 12), which anticipates instant claim 49.

In Figure 2 and page 992, Jiang et al. teach that ~ 88% phosphate of the original phosphate are released from phosvitin which is equivalent to about 90% dephosphorylation, which anticipates instant claims 50-53.

Because being a substrate of a phosvitin kinase is an inherent property of the phosvitin, the above Jiang et al. teachings anticipate instant claims 62 and 74.

Since both "extracellular" and "intracellular" for PAC are considered to be intended use which has no patentable weight for the claimed composition, the above Jiang et al. teachings anticipate instant claim 72.

Since the claim 79 recitation *"for contacting ..."* is an intended use which has no patent weight; and thus, the above Jiang et al. teachings anticipate instant claim 79.

The alkaline-dephosphorylation produced heterologous population of dephosphorylated phosvitin polypeptides, which meets the limitation of instant claim 80.

Claim 81 is rejected under 35 U.S.C. 102(b) as being anticipated by Pierce (*Instructions for GelCode Phosphoprotein staining kit* (2001, March) pages 1-3).

Pierce teaches a kit comprising an EPAC molecule, e.g., phosvitin, wherein reagents of the kit comprising said molecule is packed in separated vials (containers), e.g., "*each phosphoprotein control vial*" (see page 2, line 3). The above teaching anticipates instant claim 81.

Note that the claim 81 recitation "*for contacting a cell...*" is considered to be an intoned use which has no patentable weight for the claimed kit composition.

Claim Rejections - 35 USC §103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 46-47, 49, 62, 71-72, 74 and 79 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mckay D. W. (US Pat. No. 6569839 B1) in view of the Kipping et al. (*Biochemistry* (2001) 40, 7957-7963) with regard to the phosphorylation at residue (Thr 45).

On column 10, lines 25-35, Mckay teaches a pharmaceutical composition comprising phosvitin, as applied to instant claims 46-47.

Since obtained the phosvitin from chicken egg yolk is an ordinary approach known by the one skilled in the art, the above Mckay's teaching is applied to instant claim 49.

Said composition also comprises *hirudin* (see column 10, line 31) which is a plasma polypeptide acting as an anticoagulant, i.e., the composition comprises the phosvitin mixed with hirudin plasma protein.

Since being a substrate of a phosvitin kinase is an inherent property of the phosvitin, as applied to instant claims 62 and 74.

Since both "extracellular" and "intracellular" (for PAC) are considered to be intended use which has no patentable weight for the claimed composition, the above Mckay et al. teachings are applied to instant claim 72.

Since the claim 79 recitation *"for contacting ..."* is an intended use which has no patent weight; and thus, the above Mckay et al. teachings are applied to instant claim 79.

McKay teaches that their composition can be formulated as an emulsion form (see column 10, line 48). Because cream is a type of water-in-oil emulsion, the Mckay's teaching is applied to instant claim 71.

Mckay dose not set forth example or/and discloses the above said composition comprising the phosvitin in the patent claims.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to prepared the pharmaceutical composition comprising the phosvitin and plasma protein, e.g., hirudin. One skilled in the art would have been motivated to do this because Mckay has taught in detail as to how to formulate their pharmaceutical composition, and has taught that the hirudin acts as an anticoagulant (column 10, line 26) and the composition comprising the

hirudin is useful for treating a disorder state, e.g., bogy wound (see column 15, lines 33-35), and that the composition also comprises phosvitin (see above statement). Further, Mckay also taught that their formulation is not necessarily completely dissolved in the carrier (see column 10, lines 46-48), i.e., the formulation is in an emulsion form (e.g., cream), which is particularly applicable for treating the bogy wound. Therefore, the skilled artisan would have prepared the composition acceding to the Mckay's teaching. Claimed invention was thus *prima facie* obvious to make and use the invention at the time it was made.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Samuel Wei Liu whose telephone number is 571-272-0949. The examiner can normally be reached from 9:00 a.m. to 5:00 p.m. on weekdays. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon Weber, can be reached on 571-272-0925. The fax phone number for the organization where this application or proceeding is assigned is 703 308-4242 or 703 872-9306 (official) or 703 872-9307 (after final). Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703 305-4700.

SWL

Samuel W. Liu, Ph.D.
Patent Examiner, Art Unit 1653
May 3, 2006

JON WEBER
SUPERVISORY PATENT EXAMINER